Amendments to the Specification

Please replace the subheading at page 23, line 15, with the following amended subheading:

~~(S)-1-(2'-Chloroacetyl)pyrrolidine-2-carbonitrile~~ (S)-1-(2-Chloroacetyl)pyrrolidine-2-carbonitrile

Please replace the subheading at page 23, line 24, with the following amended subheading:

~~(R)-1-(2'-Chloroacetyl)pyrrolidine-2-carbonitrile~~ (R)-1-(2-Chloroacetyl)pyrrolidine-2-carbonitrile

Please replace the subheading at page 24, line 8, with the following amended subheading:

~~(S)-3-(2'-Chloroacetyl)thiazolidine-4-carbonitrile~~ (S)-3-(2-Chloroacetyl)thiazolidine-4-carbonitrile

Please replace the subheading at page 25, line 12, with the following amended subheading:

~~(S)-1-(2'-Chloroacetyl)azetidine-2-carbonitrile~~ (S)-1-(2-Chloroacetyl)azetidine-2-carbonitrile

Please replace the subheading at page 26, line 5, with the following amended subheading:

~~(S)-1-(2'-Bromo-2'-phenylacetyl)pyrrolidine-2-carbonitrile~~ (S)-1-(2-Bromo-2-phenylacetyl)pyrrolidine-2-carbonitrile

Please replace (Table 1) at page 27 with the following amended (Table 1):

(Table 1)

Intermediate Example	Compound Name	ESI/MS(m/z)
6	~~3-(2'-chloroacetyl)thiazolidine~~ 3-(2-chloroacetyl)thiazolidine	166 $(M+H)^+$ 164 $(M-H)^-$
7	~~1-(2'-chloroacetyl)pyrrolidine~~ 1-(2-chloroacetyl)pyrrolidine	148 $(M+H)^+$ 146 $(M-H)^-$
8	~~1-(2'-chloroacetyl)piperazine-2-carbonitrile~~ 1-(2-chloroacetyl)piperazine-2-carbonitrile	187 $(M+H)^+$ 185 $(M-H)^-$
9	~~1-(2'-chloroacetyl)morpholine~~ 1-(2-chloroacetyl)morpholine	164 $(M+H)^+$ 162 $(M-H)^-$

Please replace the paragraph at page 28, lines 17-20, with the following amended paragraph:

In a similar procedure as employed in the Intermediate Examples 3 and 10, a hydrochloride (4.4 g, Y.: 69%) of the title compound was obtained from ~~pyrrolidine-2-carboxylic~~ piperidine-2-carboxylic acid (15 g).

Please replace the paragraph at page 29, line 13 – page 30, line 2, with the following amended paragraph:

The t-butyl (2-amino-2-methyl-1-propyl)carbamate (7.9 g) obtained above, sodium iodide (8.7 g), and potassium carbonate (8.0 g) were suspended in acetone (230 ml). A solution of ~~(S)-1-(2'-chloroacetyl)~~ (S)-1-(2-chloroacetyl) pyrrolidine-2-carbonitrile (10 g) in acetone (80 ml) was added thereto with ice cooling, and stirred as such for 30 minutes. The reaction mixture was stirred for 15 hours at room temperature and then concentrated under reduced pressure. The residue was dissolved

in chloroform, then insolubles were removed by filtration, and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (eluting solvent; dichloromethane : methanol 80 : 1 → 60 : 1 → 40 : 1) to give t-butyl (S)-{2-[(2-cyanopyrrolidine-1-yl)-2-oxoethylamino]-2-methyl-1-propyl} carbamate (12 g, Y.: 91%).

Please replace the paragraphs at page 36, line 9 – page 37, line 19, with the following amended paragraphs:

3-Amino-5-methylpyrazole (970 mg) and diethyl acetomalonate (2.0 g) were dissolved in acetic acid (5 ml) and stirred for 3 hours at 120°C. The reaction mixture was cooled to room temperature and concentrated under reduced pressure, and ethanol was added to the residue which were then cooled to 0°C. Precipitated crystals were collected by filtration and washed with cold ethanol. The crystals were dried under reduced pressure to give ethyl ~~7-hydroxy-2,5-dimethyl-1,3a-dihydropyrazolo[1,5-a]pyrimidine-6-carboxylate~~ 7-hydroxy-2,5-dimethylpyrazolo[1,5-a]pyrimidine-6-carboxylate (2.2 g, Y.: 95%) as white crystals.

^{1}H NMR; (DMSO-d_6) δ (ppm): 1.3 (3H, t), 2.3 (3H, s), 2.4 (3H, s), 4.2 (2H, q), 6.0 (1H, s), 12.6 (1H, brs).

ESI/MS (m/z): 236 $(M+H)^+$, 234 $(M-H)^-$.

The ethyl ~~7-hydroxy-2,5-dimethyl-1,3a-dihydropyrazolo[1,5-a]pyrimidine-6-carboxylate~~ 7-hydroxy-2,5-dimethylpyrazolo[1,5-a]pyrimidine-6-carboxylate (235 mg) obtained above was suspended in acetone (5 ml), and potassium carbonate (138 mg) was added thereto and stirred for 30 minutes at room temperature. Methyl iodide (1.0 ml) was added to the mixture which was then refluxed for 2 hours. The reaction mixture was cooled to room temperature, then water was added to the reaction mixture which was extracted with chloroform, and the organic phase was washed with a saturated saline solution and dried over sodium sulfate anhydrous. The resulting product was concentrated under reduced pressure, and the resulting crystals were dissolved in ethanol (5 ml). 5 N Sodium hydroxide solution (1 ml) was added thereto

and stirred for 1 hour at 50°C. The reaction mixture was cooled to room temperature, and water was added to the mixture which was then washed with ethyl acetate. 2 N Hydrochloric acid was added to the aqueous phase until it became acidic, and precipitated crystals were collected by filtration and washed with water and n-hexane. The crystals were dried under reduced pressure to give the title compound (162 mg, Y.: 73%) as white crystals.

^{1}H NMR; (DMSO-d_6) δ (ppm): 2.3 (3H, s), 2.7 (3H, s), 3.7 (3H, s), 6.4 (1H, s).

ESI/MS (m/z): 222 $(M+H)^+$.

Please replace the paragraphs at page 42, line 8 - page 43, line 16, with the following amended paragraphs:

3-Amino-5-phenylpyrazole (1.56 mg) and diethyl acetomalonate (2.00 g) were dissolved in acetic acid (5.0 ml) and stirred for 3 hours at 120°C. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. Ethanol was added to the residue which were then cooled to 0°C. Precipitated crystals were collected by filtration and washed with cold ethanol. The crystals were dried under reduced pressure to give ethyl ~~7-hydroxy-5-dimethyl-2-phenyl-1,3a-dihydropyrazolo[1,5-a]pyrimidine-6-carboxylate~~ 7-hydroxy-5-methyl-2-phenylpyrazolo[1,5-a]pyrimidine-6-carboxylate (2.73 g, Y.: 92%) as white crystals.

^{1}H NMR; (DMSO-d_6) δ (ppm): 1.3 (3H, t), 2.4 (3H, s), 4.3 (2H, q), 6.7 (1H, s), 7.4 (2H, t), 7.5 (2H, t), 8.0 (1H, d).

The ethyl ~~7-hydroxy-5-dimethyl-2-phenyl-1,3a-dihydropyrazolo[1,5-a]pyrimidine-6-carboxylate~~ 7-hydroxy-5-methyl-2-phenylpyrazolo[1,5-a]pyrimidine-6-carboxylate (297 mg) obtained above was suspended in acetone (5 ml), and potassium carbonate (138 mg) was added thereto and stirred for 30 minutes at room temperature. Methyl iodide (1.0 ml) was added to the mixture which was then refluxed for 2 hours. The reaction mixture was cooled to room temperature, and water was added to the reaction mixture which was extracted with chloroform, and the organic phase was washed with a saturated saline solution and dried over sodium sulfate anhydrous. The

product was concentrated under reduced pressure, and the resulting crystals were dissolved in ethanol (5 ml). 5 N Sodium hydroxide solution (1 ml) was added thereto and stirred for 1 hour at 50°C. The reaction mixture was cooled to room temperature, and water was added to the mixture which was then washed with ethyl acetate. 2 N Hydrochloric acid was added to the aqueous phase until it became acidic, and precipitated crystals were collected by filtration and washed with water and n-hexane. The crystals were dried under reduced pressure to give the title compound (121 mg, Y.: 45%) as white crystals.

^{1}H NMR; (DMSO-d_6) δ (ppm): 2.7 (3H, s), 3.8 (3H, s), 7.2 (1H, s), 7.5 (1H, t), 7.5 (2H, dd), 8.0 (2H, d), 13.5 (1H, brs).

Please replace the paragraphs at page 43, line 20 - page 44, line 11, with the following amended paragraphs:

Triethylamine (2.02 g) and benzyloxycarbonyl chloride (1.71 g) were added dropwise to a solution of 3-amino-5-methylpyrazole (971 mg) in chloroform (20 ml) at 0°C, and the mixture was stirred for 18 hours. The mixture was concentrated under reduced pressure, and the residue was purified by column chromatography (eluting solvent; n-hexane : ethyl acetate 2 : 1) to give benzyl ~~(5-methyl-2H-pyrazol-3-yl)carbamate~~ 5-methyl-2H-pyrazol-3-ylcarbamate (1.65 g, Y.: 67%).

A mixed solution of the benzyl ~~(5-methyl-2H-pyrazol-3-yl)carbamate~~ 5-methyl-2H-pyrazol-3-ylcarbamate (600 mg) obtained above and diethyl ethoxymethylenemalonate (1.80 g) was stirred for 18 hours at 100°C. The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography (eluting solvent; n-hexane : ethyl acetate 3 : 1) to give diethyl 2-(5-benzyloxycarbonylamino-3-methylpyrazol-1-ylmethylene)malonate (700 mg, Y.: 67%).

Please replace the paragraph at page 45, lines 5 - 10, with the following amended paragraph:

In a similar procedure as employed in the Intermediate Example 24, ethyl ~~7-methoxymethylpyrazolo[1,5-a]pyrimidine-6-carboxylate~~ 7-methoxy-2-methylpyrazolo[1,5-a]pyrimidine-6-carboxylate was hydrolyzed to give the title compound.

^{1}H NMR; (DMSO-d_6) δ (ppm): 2.3 (3H, s), 6.3 (1H, s), 8.8 (1H, s).

Please replace the subheading at page 59, lines 22 - 23, with the following amended subheading:

~~1-(2,2-Dimethyl)propyl-5-methoxy-1H-indole-3-carboxylic acid~~ 1-(2,2-Dimethylpropyl)-5-methoxy-1H-indole-3-carboxylic acid

Please replace the paragraphs at page 59, line 24 - page 61, line 2, with the following amended paragraphs:

Methyl 5-methoxy-1H-indole-5-carboxylate (357 mg) was dissolved in N,N-dimethylformamide (17 ml). Sodium hydride (209 mg) was added thereto in three divided portions and stirred as such for 15 minutes. Neopentyl iodide (0.35 ml) was added dropwise thereto and stirred for 15 hours at 80°C. The reaction mixture was diluted with ethyl acetate, and the organic phase was washed with 2 N hydrochloric acid, a saturated sodium bicarbonate solution and a saturated saline solution. The resulting product was dried over sodium sulfate anhydrous and then concentrated under reduced pressure. The residue was purified by preparative thin-layer chromatography (developing solvent; ethyl acetate : n-hexane 1 : 3) to give neopentyl ~~1-(2,2-dimethyl)propyl-5-methoxy-1H-indole-3-carboxylate (114 mg, Y.: 20%) and~~

~~methyl 1-(2,2-dimethyl)propyl-5-methoxy-1H-indole-3-carboxylate (130 mg, Y.: 27%)~~ 1-(2,2-dimethylpropyl)-5-methoxy-1H-indole-3-carboxylate (114 mg, Y.: 20%) and methyl 1-(2,2-dimethylpropyl)-5-methoxy-1H-indole-3-carboxylate (130 mg, Y.: 27%).

1,4-Dioxane (2.5 ml) and 1 N sodium hydroxide solution (2.5 ml) were added to the neopentyl ~~1-(2,2-dimethyl)propyl-5-methoxy-1H-indole-3-carboxylate~~ 1-(2,2-dimethylpropyl)-5-methoxy-1H-indole-3-carboxylate (114 mg) obtained above, and the mixture was stirred for 15 hours at 40°C. Ethanol (3 ml) was added thereto and the mixture was stirred for 24 hours at 70°C. The reaction mixture was acidified by 2 N hydrochloric acid and extracted with chloroform. The extract was dried over sodium sulfate anhydrous and then concentrated under reduced pressure to give the title compound (73 mg, Y.: 81%).

^{1}H NMR; (DMSO-d_6) δ (ppm): 0.9 (9H, s), 3.7 (3H, s), 4.0 (2H, s), 6.8 (1H, dd), 7.4 (1H, d), 7.5 (1H, d), 7.8 (1H, s).

ESI/MS (m/z): 262 $(M+H)^+$, 260 $(M-H)^-$.

Please replace the subheading at page 61, line 4, with the following amended subheading:

~~1-(2,2-Dimethyl)propyl-5-methyl-1H-indole-3-carboxylic acid~~ 1-(2,2-Dimethylpropyl)-5-methyl-1H-indole-3-carboxylic acid

Please replace the subheading at page 61, lines 12 - 13, with the following amended subheading:

~~1-(2,2-Dimethyl)propyl-5-hydroxy-1H-indole-3-carboxylic acid~~ 1-(2,2-Dimethylpropyl)-5-hydroxy-1H-indole-3-carboxylic acid

Please replace the paragraph at page 61, lines 14 - 25, with the following amended paragraph:

~~1-(2,2-Dimethyl)propyl-5-methoxy-1H-indole-3-carboxylic acid~~1-(2,2-Dimethylpropyl)-5-methoxy-1H-indole-3-carboxylic acid (102 mg) was dissolved in dichloromethane (3 ml) and cooled to -78°C. 1 M Boron tribromide solution in dichloromethane (1.2 ml) was added slowly dropwise thereto, and the mixture was stirred for 1 hour while the temperature was returned from -78°C to 0°C. The reaction mixture was diluted with chloroform and alkalinized by 1 N sodium hydroxide solution, and the organic phase was separated. The aqueous phase was acidified by 2 N hydrochloric acid, extracted with chloroform and dried over sodium sulfate anhydrous. The product was concentrated under reduced pressure to give the title compound (78 mg, Y.: 80%).

Please replace the paragraphs at page 64, line 19 – page 65, line 20, with the following amended paragraphs:

1H-Indole-5-carboxylic acid (2.0 g) was dissolved in N,N-dimethylformamide (15 ml). Benzyl chloride (1.53 ml) and calcium carbonate (3.4 g) were added to the solution and stirred for 39 hours at room temperature. The mixture was diluted with ethyl acetate, and the organic phase was washed with 2 N hydrochloric acid, a saturated sodium bicarbonate solution and a saturated saline solution. The resulting product was dried over sodium sulfate anhydrous and then concentrated under reduced pressure. Precipitated solids were collected by filtration, washed with n-hexane and dried under reduced pressure to give ~~benzyl indole-5-carboxylate~~ 1H-benzyl indole-5-carboxylate (2.6 g, Y.: 85%).

^{1}H NMR; (DMSO-d_6) δ (ppm): 5.3 (2H, s), 6.6 (1H, s), 7.3-7.5 (7H, m), 7.7 (1H, d), 8.3 (1H, s), 11.5 (1H, brs).

ESI/MS (m/z): 252 $(M+H)^+$, 250 $(M-H)^-$.

The ~~benzyl indole-5-carboxylate~~ 1H-benzyl indole-5-carboxylate (1.0 g) obtained above was dissolved in N,N-dimethylformamide (10 ml). After the solution was cooled to 0°C, sodium hydride (0.32 g) was added to the solution which was then stirred for 30 minutes. Acetyl chloride (1.3 ml) was added thereto, and the mixture was stirred for 8 hours at room temperature. The reaction mixture was diluted with ethyl acetate, and the organic phase was washed with 2 N hydrochloric acid, a saturated sodium bicarbonate solution and a saturated saline solution. The organic phase was dried over sodium sulfate anhydrous and concentrated under reduced pressure. The residue was purified by column chromatography (eluting solvent; ethyl acetate : n-hexane 1 : 7 → 1 : 4) to give benzyl 1-acetyl-1H-indole-5-carboxylate (1.1 g, Y. 97%).

Please replace (Table 21) at page 111 with the following amended (Table 21):

(Table 21)

Example	A	D	n	R1	R2	R^3	R^4	E	ESI/MS (m/z)
117	quinolin-3-yl	-CONH-	1	H	H	H	H	$-SCH_2-$	345 $(M+H)^+$
118	quinolin-3-yl	-CONH-	1	H	H	H	H	$-CH_2CH_2-$	327 $(M+H)^+$
119	quinolin-3-yl	-CONH-	1	H	H	H	CN	$-CH_2CH_2CH_2-$	366 $(M+H)^+$
120	quinolin-3-yl	-CONH-	1	H	H	H	H	$-CH_2OCH_2-$	343 $(M+H)^+$
121	quinolin-2-yl	-CONH-	1	H	H	H	CN	$-CH_2CH_2-$	352 $(M+H)^+$
122	1, 3-dimethyl-1H-pyrazolo[3, 4-b]~~pyrimidin~~ pyridin-5-yl	-CONH-	1	H	H	H	CN	$-CH_2CH_2-$	370 $(M+H)^+$
123	1, 3-dimethyl-1H-pyrazolo[3, 4-b]~~-pyrimidin~~ pyridin-5-yl	-CONH-	1	H	H	H	H	$-SCH_2-$	363 $(M+H)^+$
124	1, 3-dimethyl-1H-pyrazolo[3, 4-b]~~-pyrimidin~~ pyridin-5-yl	-CONH-	1	H	H	H	H	$-CH_2CH_2-$	345 $(M+H)^+$
125	1, 3-dimethyl-1H-pyrazolo[3, 4-b]~~-pyrimidin~~ pyridin-5-yl	-CONH-	1	H	H	H	H	$-CH_2OCH_2-$	361 $(M+H)^+$
126	5-oxo-2, 3-dihydro-5H-thiazolo[3, 2-a]pyrimidin-6-yl	-CONH-	1	H	H	H	CN	$-CH_2CH_2-$	377 $(M+H)^+$
127	5-oxo-2, 3-dihydro-5H-thiazolo[3, 2-a]pyrimidin-6-yl	-CONH-	1	H	H	H	H	$-SCH_2-$	370 $(M+H)^+$
128	5-oxo-2, 3-dihydro-5H-thiazolo[3, 2-a]pyrimidin-6-yl	-CONH-	1	H	H	H	H	$-CH_2CH_2-$	352 $(M+H)^+$
129	5-oxo-2, 3-dihydro-5H-thiazolo[3, 2-a]pyrimidin-6-yl	-CONH-	1	H	H	H	CN	$-CH_2CH_2CH_2-$	391 $(M+H)^+$
130	5-oxo-2, 3-dihydro-5H-thiazolo[3, 2-a]pyrimidin-6-yl	-CONH-	1	H	H	H	H	$-CH_2OCH_2-$	368 $(M+H)^+$
131	2, 7-dimethylpyrazolo[1, 5-a]-pyrimidin-6-yl	-CONH-	1	H	H	H	CN	$-CH_2CH_2-$	370 $(M+H)^+$
132	2, 7-dimethylpyrazolo[1, 5-a]-pyrimidin-6-yl	-CONH-	1	H	H	H	H	$-SCH_2-$	363 $(M+H)^+$
133	2, 3-dihydrobenzo[1, 4]dioxan-6-yl	-CONH-	1	H	H	H	CN	$-CH_2CH_2-$	359 $(M+H)^+$
134	2, 3-dihydrobenzo[1, 4]dioxan-6-yl	-CONH-	1	H	H	H	H	$-SCH_2-$	352 $(M+H)^+$
135	2-methylimidazo[1, 2-a]-pyridin-3-yl	-CONH-	1	H	H	H	CN	$-CH_2CH_2-$	355 $(M+H)^+$